

Amendments to the Specification:

Please insert the following paragraphs at page 34, line 5 after
“(http://www.sanger.ac.uk/DataSearch/gg_search.shtml) (Table 2)” and before “As shown in
Table 2, ...” as with the following amended paragraph:

-- The sequence of the V_H region of the DP47 germ line is as follows (SEQ ID Nos:113
and 114):

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
E	V	Q	L	L	E	S	G	G	G	L	V	Q	P	G
gag	gtg	cag	ctg	ttg	gag	tct	ggg	gga	ggc	ttg	gta	cag	cct	ggg
16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
G	S	L	R	L	S	C	A	A	S	G	F	T	F	S
ggg	tcc	ctg	aga	ctc	tcc	tgt	gca	gcc	tct	gga	ttc	acc	ttt	agc
31	32	33	34	35	36	37	38	39	40	41	42	43	44	45
S	Y	A	M	S	W	V	R	Q	A	P	G	K	G	L
agc	tat	gcc	atg	agc	tgg	gtc	cgc	cag	gct	cca	ggg	aag	ggg	ctg
46	47	48	49	50	51	52	53	54	55	56	57	58	59	60
E	W	V	S	A	I	S	G	S	G	G	S	T	Y	Y
gag	tgg	gtc	tca	gct	att	agt	ggg	agt	ggg	ggg	agc	aca	tac	tac
61	62	63	64	65	66	67	68	69	70	71	72	73	74	75
A	D	S	V	K	G	R	F	T	I	S	R	D	N	S
gca	gac	tcc	gtg	aag	ggc	cgg	ttc	acc	atc	tcc	aga	gac	aat	tcc
76	77	78	79	80	81	82	83	84	85	86	87	88	89	90
K	N	T	L	Y	L	Q	M	N	S	L	R	A	E	D
aag	aac	acg	ctg	tat	ctg	caa	atg	aac	agc	ctg	aga	gcc	gag	gac
91	92	93	94	95	96	97	98	99						
T	A	V	Y	Y	C	A	K	.						
acg	gcc	gta	tat	tac	tgt	gcg	aaa	ga						

The sequence of the VL region from the DPK15 germ line is as follows (SEQ ID
Nos:115 and 116):

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
D	I	V	M	T	Q	S	P	L	S	L	P	V	T	P
GAT	ATT	GTG	ATG	ACT	CAG	TCT	CCA	CTC	TCC	CTG	CCC	GTC	ACC	CCT

16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
G	E	P	A	S	I	S	C	R	S	S	Q	S	L	L
GGA	GAG	CCG	GCC	TCC	ATC	TCC	TGC	AGG	TCT	AGT	CAG	AGC	CTC	CTG
31	32	33	34	35	36	37	38	39	40	41	42	43	44	45
H	S	N	G	Y	N	Y	L	D	W	Y	L	Q	K	P
CAT	AGT	AAT	GGA	TAC	AAC	TAT	TTG	GAT	TGG	TAC	CTG	CAG	AAG	CCA
46	47	48	49	50	51	52	53	54	55	56	57	58	59	60
G	Q	S	P	Q	L	L	I	Y	L	G	S	N	R	A
GGG	CAG	TCT	CCA	CAG	CTC	CTG	ATC	TAT	TTG	GGT	TCT	AAT	CGG	GCC
61	62	63	64	65	66	67	68	69	70	71	72	73	74	75
S	G	V	P	D	R	F	S	G	S	G	S	G	T	D
TCC	GGG	GTC	CCT	GAC	AGG	TTC	AGT	GGC	AGT	GGA	TCA	GGC	ACA	GAT
76	77	78	79	80	81	82	83	84	85	86	87	88	89	90
F	T	L	K	I	S	R	V	E	A	E	D	V	G	V
TTT	ACA	CTG	AAA	ATC	AGC	AGA	GTG	GAG	GCT	GAG	GAT	GTT	GGG	GTT
91	92	93	94	95	96	97	98	99	100	101				
Y	Y	C	M	Q	A	L	Q	T	P	P				
TAT	TAC	TGC	ATG	CAA	GCT	CTA	CAA	ACT	CCT	CCT	---			

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Previously presented) An isolated MUC1-specific binding member comprising an amino acid sequence of the formula:

X₁ X₂ His Thr Gly X₃ Gly Val Trp X₄ Pro X₅ X₆ X₇ (SEQ ID NO: 28),

wherein X₁ is Ala, Ser, Thr, or Val;

X₂ is Lys, Ile Arg, or Gln;

X₃ is Gly, Arg, Val, Glu, Ser, or Ala;

X₄ is Asp or Asn;

X₅ is Ile, Leu, Met, Phe, or Val;

X₆ is Asp, Gly, Lys, Asn, Ala, His, Arg, Ser, Val, or Tyr; and

X₇ is Tyr, His, Lys, Asn, Asp, Ser, Pro,

wherein the amino acid sequences is in its germline framework or is in a framework from a different polypeptide and the isolated MUC1-specific binding member binds MUC1.

2. (Previously presented) The MUC1-specific binding member according to Claim 1, wherein the MUC1-specific binding member comprises an amino acid sequence selected from the group consisting of:

Ala Lys His Thr Gly Gly Gly Val Trp Asp Pro Ile Asp Tyr (amino acids 97-110 of SEQ ID NO:3);

Ala Lys His Thr Gly Arg Gly Val Trp Asp Pro Ile Gly Tyr (SEQ ID NO:29);

Ala Lys His Thr Gly Gly Gly Val Trp Asp Pro Ile Lys His (SEQ ID NO:30);

Ala Lys His Thr Gly Gly Gly Val Trp Asp Pro Ile Gly Tyr (SEQ ID NO:31); and

Ala Ile His Thr Gly Gly Gly Val Trp Asp Pro Ile Lys Tyr (SEQ ID NO:32).

3. (Previously presented) An isolated MUC1-specific binding member comprising an antigen binding domain of SEQ ID NO:1 and an antigen binding domain of SEQ ID NO:3, wherein the isolated MUC1-specific binding member binds MUC1.

4. (Currently amended) A MUC1-specific binding member comprising a CDR having an amino acid sequence selected from the group consisting of amino acids 24 to 39 of SEQ ID NO:1, amino acids 55 to 61 of SEQ ID NO:1, amino acids 94 to 102 of SEQ ID NO:1, amino acids 31 to 35 of SEQ ID NO:3, amino acids 50 to 66 of SEQ ID NO:3, amino acids 99 to 110 of SEQ ID NO:3, and conservatively substituted sequences of ~~any of the preceding sequences~~ amino acids 99 to 110 of SEQ ID NO:3, wherein the amino acid sequence is in its germline framework or is in a framework from a different polypeptide and the isolated MUC1-specific binding member binds MUC1.

5. (Original) The MUC1-specific binding member according to any of Claims 1, 2, 3, or 4, wherein said MUC1-specific binding member is a fusion protein.

6. (Original) The MUC1-specific binding member according to any one of Claims 1, 2, 3, or 4, further comprising a detectable label or tag.

7. (Original) The MUC1-specific binding member according to Claim 6, wherein the detectable label or tag is selected from the group consisting of epitope tags, fluorescent labels, radioactive labels, heavy metals, anti-cancer drugs, toxins, and magnetic resonance imaging labels.

8. (Original) The MUC1-specific binding member according to any one of Claims 1, 2, 3, or 4, wherein the MUC1-specific binding member is an antibody molecule selected from the group consisting of immunoglobulins, Fab antibodies, F(ab')₂ antibodies, diabodies, scFv

antibodies, double scFv, Fv molecules, dAb, immunocytokine molecules, and immunotoxin molecules.

9. (Previously presented) The MUC1-specific binding member according to Claim 8, wherein the MUC1-specific binding member is an immunocytokine molecule and the immunocytokine molecule comprises an amino acid sequence of SEQ ID NO:5.

10. (Previously presented) The MUC1-specific binding member according to Claim 9, further comprising a detectable label or tag.

11. (Original) The MUC1-specific binding member according to Claim 10, wherein the detectable label or tag is selected from the group consisting of, epitope tags, fluorescent labels, radioactive labels, and magnetic resonance imaging labels.

12. (Previously presented) The MUC1-specific binding member according to Claim 8, wherein the MUC1-specific binding member is an immunoglobulin and the immunoglobulin comprises a light chain polypeptide comprising the amino acid sequence of SEQ ID NO:24 and a heavy chain polypeptide comprising the amino acid sequence of SEQ ID NO:26.

13. (Previously presented) The MUC1-specific binding member according to Claim 12, further comprising a detectable label or tag.

14. (Original) The MUC1-specific binding member according to Claim 13, wherein the detectable label or tag is selected from the group consisting of enzymes, epitope tags, fluorescent labels, radioactive labels, heavy metals, anti-cancer drugs, toxins, and magnetic resonance imaging labels.

15. (Previously presented) A MUC1-specific binding member comprising a heavy chain variable region, or CDR thereof, from the DP47 germ line wherein the MUC1-specific binding member binds MUC1.

16. (Previously presented) A MUC1-specific binding member comprising a light chain variable region, or a CDR thereof, from the DPK15 germ line wherein the MUC1-specific binding member binds MUC1.

17. (Previously presented) A MUC1-specific binding member comprising a heavy chain variable region, or CDR thereof, from the DP47 germ line and a light chain variable region, or CDR thereof, from the DPK15 germ line wherein the MUC1-specific binding member binds MUC1.

18. (Currently amended) A MUC1-specific binding member comprising an amino acid sequence that is about 70% or more homologous to an amino acid sequence from the group consisting of:

Ala Lys His Thr Gly Gly Gly Val Trp Asp Pro Ile Asp Tyr (amino acids 97-110 of SEQ ID NO:3);

Ala Lys His Thr Gly Arg Gly Val Trp Asp Pro Ile Gly Tyr (SEQ ID NO:29);

Ala Lys His Thr Gly Gly Gly Val Trp Asp Pro Ile Lys His (SEQ ID NO:30);

Ala Lys His Thr Gly Gly Gly Val Trp Asp Pro Ile Gly Tyr (SEQ ID NO:31);

Ala Ile His Thr Gly Gly Gly Val Trp Asp Pro Ile Lys Tyr (SEQ ID NO:32);

~~amino acids 24 to 39 of SEQ ID NO:1;~~

~~amino acids 55 to 61 of SEQ ID NO:1;~~

~~amino acids 94 to 102 of SEQ ID NO:1;~~

~~amino acids 31 to 35 of SEQ ID NO:3;~~

~~amino acids 50 to 66 of SEQ ID NO:3; and~~

amino acids 99 to 110 of SEQ ID NO:3

wherein the MUC1-specific binding member binds MUC1.

19. (Previously presented) The MUC1-specific binding member of claim 18, wherein the amino acid sequence is about 80% or more homologous to any of the amino acid sequences.

20. (Previously presented) The MUC1-specific binding member of claim 18, wherein the amino acid sequence is about 90% or more homologous to any of the amino acid sequences.

21. (Previously presented) The MUC1-specific binding member of claim 18, wherein the amino acid sequence is about 95% or more homologous to any of the amino acid sequences.

22. (Previously presented) The MUC1-specific binding member of claim 18, wherein the amino acid sequence is about 97% or more homologous to any of the amino acid sequences.

23. (Previously presented) The MUC1-specific binding member of claim 18, wherein the amino acid sequence is about 99% or more homologous to any of the amino acid sequences.

24. (Currently amended) A polypeptide molecule comprising an amino acid sequence that is about 70% or more homologous to ~~an amino acid sequence selected from the group consisting of amino acids 24 to 39 of SEQ ID NO:1, amino acids 55 to 61 of SEQ ID NO:1, amino acids 94 to 102 of SEQ ID NO:1, amino acids 31 to 35 of SEQ ID NO:3, amino acids 50 to 66 of SEQ ID NO:3, amino acids 99 to 110 of SEQ ID NO:3, and SEQ ID NO:5,~~ wherein the polypeptide molecule binds MUC1.

25. (Currently amended) A polypeptide molecule comprising an amino acid sequence that is about 80% or more homologous to ~~an amino acid sequence selected from the group consisting of amino acids 24 to 39 of SEQ ID NO:1, amino acids 55 to 61 of SEQ ID NO:1, amino acids 94 to 102 of SEQ ID NO:1, amino acids 31 to 35 of SEQ ID NO:3, amino acids 50~~

~~to 66 of SEQ ID NO:3, amino acids 99 to 110 of SEQ ID NO:3, and SEQ ID NO:5 wherein the polypeptide molecule binds MUC1.~~

26. (Currently amended) A polypeptide molecule comprising an amino acid sequence that is about 90% or more homologous to ~~an amino acid sequence selected from the group consisting of SEQ ID NO:1, amino acids 24 to 39 of SEQ ID NO:1, amino acids 55 to 61 of SEQ ID NO:1, amino acids 94 to 102 of SEQ ID NO:1, SEQ ID NO:3, amino acids 31 to 35 of SEQ ID NO:3, amino acids 50 to 66 of SEQ ID NO:3, amino acids 99 to 110 of SEQ ID NO: 3, and SEQ ID NO:5,~~ wherein the polypeptide molecule binds MUC1.

27. (Currently amended) A polypeptide molecule comprising an amino acid sequence that is about 95% or more homologous to ~~an amino acid sequence selected from the group consisting of SEQ ID NO:1, amino acids 24 to 39 of SEQ ID NO:1, amino acids 55 to 61 of SEQ ID NO:1, amino acids 94 to 102 of SEQ ID NO:1, SEQ ID NO:3, amino acids 31 to 35 of SEQ ID NO:3, amino acids 50 to 66 of SEQ ID NO:3, amino acids 99 to 110 of SEQ ID NO:3, and SEQ ID NO:5,~~ wherein the polypeptide molecule binds MUC1.

28. (Currently amended) A The polypeptide molecule according to any of claims 24, 25, 26 or 27, further comprising ~~an amino acid sequence that is about 97% or more homologous to~~ an amino acid sequence selected from the group consisting of SEQ ID NO:1, amino acids 24 to 39 of SEQ ID NO:1, amino acids 55 to 61 of SEQ ID NO:1, amino acids 94 to 102 of SEQ ID NO:1, SEQ ID NO:3, amino acids 31 to 35 of SEQ ID NO:3, and amino acids 50 to 66 of SEQ ID NO:3, ~~amino acids 99 to 110 of SEQ ID NO:3, and SEQ ID NO:5,~~ wherein the polypeptide molecule binds MUC1.

29. (Currently amended) A The polypeptide molecule according to claim 24, further comprising the following ~~an amino acid sequence~~ sequences ~~that is about 99% or more homologous to an amino acid sequence selected from the group consisting of SEQ ID NO:1,~~

amino acids 24 to 39 of SEQ ID NO:1, amino acids 55 to 61 of SEQ ID NO:1, amino acids 94 to 102 of SEQ ID NO:1, SEQ ID NO:3, amino acids 31 to 35 of SEQ ID NO:3, and amino acids 50 to 66 of SEQ ID NO:3, ~~amino acids 99 to 110 of SEQ ID NO:3, and SEQ ID NO:5,~~ wherein the polypeptide molecule binds MUC1.

30. to 69. (Previously Cancelled)

70. (Currently amended) The MUC1-specific binding member of claim 4, comprising two or more CDRs of an antibody V_L or V_H region, wherein the CDRs are selected from the group consisting of: amino acids 24 to 39 of SEQ ID NO:1 amino acids 55 to 61 of SEQ ID NO:1, amino acids 94 to 102 of SEQ ID NO:1, amino acids 31 to 35 of SEQ ID NO:3, amino acids 50 to 66 of SEQ ID NO:3, amino acids 99 to 110 of SEQ ID NO:3, and conservatively substituted sequences of ~~any of the preceding sequences~~ amino acids 99 to 110 of SEQ ID NO:3.

71. (Previously presented) The MUC1-specific binding member of claim 70, wherein the MUC1-specific binding member comprises at least two CDRs of the antibody V_L region and at least two CDRs of the antibody V_H region.

72. (Previously presented) The MUC1-specific binding member of claim 70, wherein the MUC1-binding member comprises all three CDRs of the V_L region.

73. (Previously presented) The MUC-1-specific binding member of claim 70, wherein the MUC-1 binding member comprises all three CDRs of the V_H region.

74. (Previously presented) The MUC1-specific binding member of claim 1, wherein the germline framework is a DP47 framework, a DPK15 framework or both.

75. (Previously presented) The isolated MUC1 specific binding member of claim 1, wherein the framework of the different polypeptide is a framework from a different germ line or a different antibody or fragments thereof.

76. (Previously presented) The isolated MUC1-specific binding member of claim 75, wherein the framework of the different polypeptide is a human framework or fragment thereof.

77. (Previously presented) The isolated MUC1-specific binding member of claim 75, wherein the framework is a framework other than a DP47 or DPK15 framework.

78. (Previously presented) The isolated MUC1-specific binding member of any of claims 3 and 4, wherein the MUC1-specific binding member is a human MUC1-specific binding member.

79. (Previously presented) The isolated MUC1-specific binding member of any of claims 1, 2, 3 and 4, wherein the MUC1-specific binding member has reduced HAMA response in humans as compared to a murine antibody.

80. (Previously presented) The polypeptide molecule according to claim 29, wherein the polypeptide molecule comprises the amino acid sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:3.

81. (Previously presented) The polypeptide molecule according to claim 80, wherein the polypeptide molecule comprises the amino acid sequence of SEQ ID NO:1 and SEQ ID NO:3.